intranasal (i.n.) administration of IAV-nanovax. Ferrets were made pre-immune via infection with an A/Singapore/6/68 (H1N1) virus. 70 days later some of the ferrets were administered IAV-nanovax [formulation contained a ferret reactive CpG sequence and HA and NP proteins from A/PR/8/34 (H1N1)]. 35 days after the initial vaccination a group of the vaccinated ferrets was boosted with another i.n. administration of the IAV-nanovax. While control pre-immune ferrets that were not vaccinated showed the expected immunity (Ab) to A/Singapore/6/68 they did not have protective titers against A/PR/8/34 or A/CA/09 (H1N1).

Pre-immune ferrets vaccinated with IAV-nanovax showed protective titers against both A/Singapore and A/PR/8/34 at day 121 of the experiment. Additionally, these ferrets showed some antibody reactivity to A/CA/09 and shed less virus and lost less weight upon subsequent challenge with A/CA/09 virus. These positive results are important since the ferret is a key pre-clinical model and humans are inherently pre-immune to a variety of influenza viruses.

Example 8. IAV-Nanovax Induces Tissue Resident Memory CD4 and CD8 T Cells and GC B Cell Responses in the Lungs and IAV-Specific Antibody in the Serum of Outbred Animals

FIG. **21** illustrates the induction of full adaptive immunity (antigen-reactive B cells, Ab, CD4 T cells, CD8 T cells) and protection against influenza challenge (both homologous and heterologous, see FIG. **7**) in outbred Swiss-Webster mice that are similar to the genetic diversity of humans after i.n. IAV-nanovax administration.

Example 9. CD103+ Lung DC Migrating from the Lungs to the Lung Draining Lymph Nodes Contain Qdot+IAV-Nanovax at 30 Hours Post Vaccination

FIG. **22** illustrates the use of nanoparticles loaded with highly fluorescent quantum dots (Qdots) we have shown the nanoparticles to be taken up by dendritic cells (DCs) and other antigen presenting cells (APCs) in the lungs, and within DCs that have migrated from the lungs into the lung draining lymph nodes. Qdot containing particles are not found in DCs in lymph nodes that do not drain the lungs (control experiment).

Further the lack of Qdot+CD11b+DC following Nanovax-Qdot vaccination indicates that the IAV-nanovax does not drain directly to the lymph nodes as such drainage would make it accessible to uptake by CD11b+DC within the lymph nodes. Finally, as a fraction of the CD11b+DC present in the lymph nodes have recently migrated from the lung interstitium to the lymph nodes, the presence of Qdot only in CD103+DC suggest that it may be selectively carried to the lymph nodes by the CD103+DC which are known to be initially positioned within the airways of the lung. These findings indicate that the IAV-nanovax easily travels to the lower airway (lung) after i.n. administration and is transported via DC through the lymphatics to the draining lymph nodes to induce local and systemic immunity.

While specific embodiments have been described above with reference to the disclosed embodiments and examples, such embodiments are only illustrative and do not limit the scope of the invention. Changes and modifications can be made in accordance with ordinary skill in the art without departing from the invention in its broader aspects as defined in the following claims.

All publications, patents, and patent documents are incorporated by reference herein, as though individually incorporated by reference. No limitations inconsistent with this disclosure are to be understood therefrom. The invention has been described with reference to various specific and preferred embodiments and techniques. However, it should be understood that many variations and modifications may be made while remaining within the spirit and scope of the invention.

What is claimed is:

1. An immunogenic composition comprising:

one or more polyanhydride copolymers forming a biodegradable first polyanhydride nanoparticle, the copolymers including 1,8-bis(p-carboxyphenoxy)-3,6-dioxaoctane (CPTEG) and 1,6-bis(p-carboxyphenoxy) hexane (CPH) in a ratio of about 20:80;

an adjuvant other than CPTEG, CPH, or combinations thereof;

one or more immunogenic proteins of an Influenza Virus, the influenza Virus selected from the group consisting of Influenza A Virus, Influenza B Virus, Influenza C Virus, and Influenza D Virus wherein each of the adjuvant and the one or more immunogenic proteins are entrapped within the nanoparticle; and

an excipient.

2. The immunogenic composition of claim **1** further comprising at least a second biodegradable polyanhydride nanoparticle formed of one or more polyanhydride copolymers, the copolymers including CPTEG and CPH in a ratio of about 20:80; a second immunogenic protein of an Influenza Virus and an adjuvant within an interior of the second nanoparticle, the second immunogenic protein being different than the immunogenic protein.

3. The immunogenic composition of claim **1**, wherein the immunogenic proteins include one or more subtypes of the Influenza A virus selected from the group consisting of H1, H2, H3, H5, H7, and H9.

4. The immunogenic composition of claim **1**, wherein the immunogenic proteins include one or more of Hemagglutinin (HA), Neuraminidase (NA), Nucleocapsid Protein (NP), Matrix Protein 1 (M1), Matrix Protein 2 (M2), Polymerase Basic Protein 1 (PB1), Polymerase Basic Protein 2 (PB2), Polymerase Acidic Protein (PA), Nonstructural Proteins 1 (NS1), Nonstructural Proteins 2/Nuclear Export Protein (NS2/NEP), Polymerase Basic Protein 1 Segment Second Proteins (PB1-F2), Influenza B Virus Membrane Protein (BM2), Influenza B Virus Membrane Protein (NB), Influenza A Virus Segment 2 Alternative Splicing Protein (M42), Influenza A Virus Segment 1 Alternative Splicing Protein (PB2-S1), Influenza A Virus Segment 2 Alternative Initiation Protein (N40), Influenza A Virus Segment 3 Ribosomal Shift Protein (PA-X), Influenza A Virus Segment 3 Alternative Initiation Protein (PA-N182), Influenza A Virus Segment 3 Alternative Initiation Protein (PA-N155), Influenza C/D Virus Polymerase Complex Protein (P3), Influenza C/D Virus Surface Glycoproteins: Hemagglutinin, Esterase, and Fusion activities (HEF), Influenza C/D Virus Matrix Protein (CM1), or Influenza C/D Virus surface glycoprotein CM2.

5. The immunogenic composition of claim **1**, wherein the immunogenic proteins are selected from the group consisting of Influenza A Virus Hemagglutinin (HA) subtypes H1, H2, and H3, Influenza A Virus Neuraminidase (NA) subtypes N1 and N2, Influenza A Virus Nucleocapsid Protein (NP), Influenza A Virus Matrix Protein 1 (M1), Influenza B Virus HA and NA, Influenza A Virus HA subtypes H1 and H3, Influenza A Virus NA subtypes N1 and N2, Influenza A Virus NP, M1, Nonstructural Proteins 1 (NS1), Polymerase Acidic Protein (PA), and Polymerase Basic Protein 1 (PB1),